PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 060348/0119	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. **PCT**/IB2005/000204	International filing date *(day/month/year)* 27 January 2005	Priority date *(day/month/year)* 2 February 2004

International Patent Classification (IPC) or national classification and IPC

Int. Cl.

A61K 47/00 (2006.01)

Applicant

ENGENEIC MOLECULAR DELIVERY PTY LTD. et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of **3** sheets, as follows:
      - [ ] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

[X]	Box No. I	Basis of the report
[ ]	Box No. II	Priority
[X]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[ ]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[X]	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30 November 2005	01 March 2006
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **CHRIS LUTON** Telephone No. (02) 6283 2256

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2005/000204

Box No. I Basis of the report

1. With regard to the **language,** this report is based on:

[X] The international application in the language in which it was filed

[ ] A translation of the international application into , which is the language of a translation furnished for the purposes of:

[ ] international search (under Rules 12.3(a) and 23.1 (b))

[ ] publication of the international application (under Rule 12.4(a))

[ ] international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

[ ] the international application as originally filed/furnished

[X] the description:

pages **1-55** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

[X] the claims:

pages as originally filed/furnished
pages* as amended (together with any statement) under Article 19
pages* **56-58** received by this Authority on **18 February 2006** with the letter of **18 February 2006**
pages* received by this Authority on with the letter of

[X] the drawings:

pages **1/6-6/6** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

[ ] a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. [X] The amendments have resulted in the cancellation of:

[ ] the description, pages
[X] the claims, **page 59**.
[ ] the drawings, sheets/figs
[ ] the sequence listing *(specify)*:
[ ] any table(s) related to the sequence listing *(specify)*:

4. [ ] This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

[ ] the description, pages
[ ] the claims, Nos.
[ ] the drawings, sheets/figs
[ ] the sequence listing *(specify)*:
[ ] any table(s) related to the sequence listing *(specify)*:

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos: **28**

because:

☐ the said international application, or the said claims Nos.
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos.
are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos.
are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*

☒ no international search report has been established for said claim Nos. **28 (see extra sheet)**

☐ A meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ Furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ Furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ Pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ A meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	**1-27, 29-30**	**YES**
	Claims		**NO**
Inventive step (IS)	Claims	**1-27, 29-30**	**YES**
	Claims		**NO**
Industrial applicability (IA)	Claims	**1-27, 29-30**	**YES**
	Claims		**NO**

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1 – WO 2003/033519
D2 – WO 2003/072014
D3 – SUZUKI et al.

NOVELTY (N) Claims 1-27, 29-30

D1 discloses compositions comprising intact minicells containing a therapeutic nucleic acid molecule. A therapeutic nucleic acid molecule is a drug molecule. D1 teaches the purification of minicells to a purity of fewer than one parent cell per 10^9 minicells (page 21, line 8 and examples). As the present invention utilises the same purification methods described in D1, the methods of D1 are presumed to be able to achieve the same purification levels described by the present application. However, the Applicant has restricted claims 1-27 and 29-30 to minicells comprising a small molecule drug and uses thereof. D1 does not disclose the use of minicells for the delivery of small molecule drugs. Therefore claims 1-27 and 29-30 are novel in light of the disclosure of D1.

Neither D2 nor D3 disclose minicells comprising a small molecule drug. Therefore, claims 1-27 and 29-30 are novel in light of D2 and D3.

INVENTIVE STEP (IS) Claims 1-27, 29-30

D1 discloses the use of *intact* minicells to deliver therapeutic nucleic acid molecules. Thus, D1 clearly indicates that intact minicells are capable of delivering their contents into living cells. In light of D1, the skilled addressee would have readily understood that the interior of a minicell could support similar substances to those found in the cytoplasm of bacterial cells, including proteins, nucleic acids and a range of small organic molecules. D3 further demonstrates that therapeutically useful substances may be produced within minicells.

It was submitted that it was unheralded by D1 that drugs could be delivered intracellularly without degradation. However, that is precisely what D1 demonstrates by the delivery of a therapeutic nucleic acid. Thus, D1 actually supports the suggestion that minicells may be used to deliver substances without degradation.

D2 is replete with suggestions that minicells may be used for the delivery of therapeutic substances, including both small molecule drugs and peptide drugs (see paragraphs 34, 666-669 for example). D2 exemplifies the expression of protein substances in minicells (see examples).

(continued on extra sheet ...)

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The specification does not adequately demonstrate the purification of minicells to fewer than 1 contaminating cell per 10^9 minicells. Therefore, claims 5 and 6 are not fully supported by the description.

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: Box V

However, it was submitted that the cited prior art fails to teach how to package a small molecule drug within minicells. It was submitted that the skilled addressee would have looked to the prior art and found reference only to packaging substances in minicells via **expression within the parent cell before budding.** In addition, it was submitted that this is not possible with small molecule drugs and that none of the cited prior art suggests loading minicells from an external source of drug. Consequently, claims 1-27 and 29-30 are considered to involve an inventive step in light of the cited prior art.

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: Box III

Originally-filed claims 8-38 were not searched and therefore not reported on. However, in response to the second International Preliminary Examination Opinion, claims 1-27 and 29-30 have been restricted to minicells comprising a small molecule drug and uses thereof. This restricted subject matter is considered to have been covered by the original search. Consequently, this report has been established in respect of the parts relating to claims 1-27 and 29-30.